

Epa's Virtual Embryo: Modeling Developmental Toxicity

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Embryogenesis is regulated by concurrent activities of signaling pathways organized into networks that control spatial patterning, molecular clocks, morphogenetic rearrangements and cell differentiation. Quantitative mathematical and computational models are needed to better understand how genetic errors and biochemical disruptions may perturb these complex processes, leading to developmental defects. EPA's Virtual Embryo (v-Embryo™) is an effort to build cell-based computational models using detailed knowledge of molecular embryology and data from the ToxCast™ high-throughput *in vitro* screening effort. The end goal is a library of simulations that can be manipulated *in silico* and correlated with *in vitro* responses or *in vivo* phenotypes in predictive modeling of developmental processes and toxicities. The Specific Aims of the project are to: build a virtual tissue knowledgebase (VT-KB) relevant to development; construct a virtual tissue simulation engine (VT-SE) for embryonic systems; specify rules for component interactions of developmental signaling pathways; and analyze abnormal developmental trajectories that follow perturbations. Software for these purposes includes open-access programming environments such as CompuCell3D, Python, BioTapestry and GanttPV. Initial models for proof of principle are focusing on two systems with extensive experimental embryology and targets for disruption by environmental chemicals: limb-bud development and optic cup development. The modeling effort can enhance EPA efforts applying the latest scientific knowledge in quantitative models of dose-response relationships and uncertainty analysis of developmental and reproductive toxicity. *[This work has been reviewed by EPA and cleared for presentation, but does not reflect official Agency policy].*